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REVIEW ARTICLE

Surgical management of high-grade paediatric spondylolisthesis: meta-analysis and systematic review

Robert Koucheki[1,2] · Brett Rocos[3,4] · Rajiv Gandhi[1,4] · Stephen J. Lewis[1,3] · David E. Lebel[1,3]

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Abstract

Purpose There is currently no consensus on the management of high-grade spondylolisthesis (HGS) in paediatric populations. The objective of this analysis is to compare the outcomes of reduction followed by fusion (RFF) or in situ fusion (ISF) in paediatric patients.

Methods Using major databases, a systematic literature search was performed. Primary studies comparing ISF with RFF in paediatric and adolescent patients were identified. Study data including patient-reported outcomes, complications, and spinopelvic parameters were collected and analysed.

Results Seven studies were included, comprising 97 ISF and 131 RFF. Average patient age was 14.4 ± 2.1 years and follow up was 8.2 ± 5.1 years. Patients undergoing RFF compared to patients undergoing ISF alone were less likely to develop pseudarthrosis (RR 0.51, 95% CI, [0.26, 0.99], $p = 0.05$). On average, RFF led to 11.97° more reduction in slip angle and 34.8% more reduction in sagittal translation ($p < 0.00001$) compared to ISF. There was no significant difference between patient satisfaction and pain at follow up. Neurologic complications and reoperation rates were not significantly different.

Conclusions Both RFF and ISF are effective techniques for managing HGS. Performing a reduction followed by fusion reduces the likelihood of pseudarthrosis in paediatric patients. The difference between risk of neurologic complications, need for reoperation, patient satisfaction, and pain outcomes did not reach statistical significance. Correlation with patient-reported outcomes still needs to be further explored.

Level 3 evidence Meta-analysis of Level 3 studies.

Keywords High-grade spondylolisthesis · Paediatric spondylolisthesis · Severe spondylolisthesis · Surgical management · Meta-analysis · Systematic review

Introduction

High-grade spondylolisthesis (HGS) is defined as Meyerding grade III or higher, representing a translation of at least 50% of the distal vertebral body maximal anteroposterior dimension. Factors which predict progression of a spondylolisthesis include a higher Meyerding grade and slip angle, whilst pelvic incidence and sacral inclination do not appear to be significant influences [1, 2].

Although the optimal management of symptomatic HGS remains unclear, the literature supports surgical intervention to prevent disease progression [3–7]. Surgery aims to fuse the affected vertebra and prevent further translation, however it is unclear whether performing reduction followed by fusion (RFF) or in situ fusion (ISF) is the best operative approach [8]. Although ISF has been commonly used to treat HGS, reduction allows for the restoration of spinal anatomy and may improve the likelihood of fusion [9–13].

Mac-Thiong, further classified HGS into balanced and unbalanced patterns [14]. Balanced HGS is defined as HGS with low pelvic tilt and high sacral slope, while unbalanced HGS is the opposite [14, 15]. Although reduction is theorised to increase the rate of complications, neurological

✉ David E. Lebel
david.lebel@sickkids.ca

1 Temerty Faculty of Medicine, University of Toronto, Toronto, ON, Canada

2 Institute of Biomedical Engineering, Toronto, ON, Canada

3 Department of Orthopaedic Surgery, The Hospital for Sick Children, Toronto, ON, Canada

4 Department of Orthopaedic Surgery, Toronto Western Hospital (UHN), Toronto, ON, Canada

deficit, operative time and blood loss [12], it has been recommended that unbalanced HGS would benefit from reduction to address the limited ability of the lumbar spine to achieve balance in these cases [14–17].

A previous meta-analysis has compared RFF with ISF for HGS and found that both procedures were associated with good outcomes, while reduction was found to correct the deformity, reduce translation, and not be associated with a significant increased risk of neurological complications compared to ISF alone [18]. The authors did not separate pooled data analysis for the paediatric studies.

Another meta-analysis compared ISF and reduction in both low-grade and HGS without differentiating between adult and paediatric patients [19]. The authors did not find any benefit of reduction over ISF when considering clinical satisfaction and neurological complications. Recent meta-analysis was conducted investigating the optimal management of adult HGS [20]. Both approaches were shown to be safe and effective; however, reduction was found to offer better disability relief and correction of spinopelvic parameters. Although not statistically significant, ISF had a higher volume of intra-operative blood loss and a clinically higher incidence of neurologic complications, pseudarthrosis, and infectious complications, and lower incidence of overall complications and dural tears [20].

No meta-analysis has yet limited its focus to high-grade paediatric spondylolisthesis. Paediatric spondylolisthesis is relatively rare and has a different disease aetiology compared to adult HGS; its surgical management is challenging and associated with significant morbidity even among experienced surgeons [21]. The aim of this analysis is to compare the outcomes of ISF versus RFF for HGS in paediatric patients and include the most recent studies not available to past authors.

Methods

Literature search and inclusion criteria

Using Ovid MEDLINE and Embase databases, a systematic search was performed using the keywords “spondylolisthesis” and “high-grade” OR “high grade”. Results were limited to paediatric and adolescent populations with an average participant age of less than 20 years. Filters of "human studies” and “English language” were applied. PubMed database was used to perform reference chaining. PROSPERO registration was also completed [22].

Primary studies comparing ISF with RFF were selected and only comparative level 3 studies or higher were included in the analysis. Studies needed to include one or more of the outcomes shown in Table 1. Two reviewers independently reviewed all identified studies, performed title/abstract screenings, and detailed full text analysis. Detailed reasons for exclusion are shown in Fig. 2. Data from the included studies were pooled and analysed.

Table 1 Study outcomes

Study outcomes
Subjective patient satisfaction
Low back pain or pain radiating to leg
Incidence of pseudarthrosis
Incidence of neurological complication
Wound infection
Radiographic change in slip angle and/or sagittal translation
Intraoperative blood loss
Surgical time
Re-operation rates

Finally, it should be noted that we decided to include one study on young adult patients with HGS in our analysis as their bone biology, disease aetiology (i.e. isthmic/dysplastic), and post-operative healing resembles the paediatric patients more than the adult population.

Risk of bias and quality assessment

Reviewers used the ROBINS-I tool and the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) framework, to appraise risk of bias in the included studies and to assign an overall quality rating [23].

Statistical analysis

Microsoft Excel V16.44 was used for data extraction and for descriptive statistics. The Review-Manager (RevMan)-V5.4 was used to analyse the pooled data. For dichotomous data, including subjective patient satisfaction data, development of pseudarthrosis and neurological deficits, Mantel–Haenszel statistical method with a fixed effect model was used to calculate odds ratio (OR) or risk ratio (RR) at a 95% confidence interval (CI). For continuous data, the inverse variance statistical method with fixed effect model was utilized to calculate the mean difference and 95% CIs. In cases with high heterogeneity a random effect model was substituted. I^2 tests were used as measures for heterogeneity: [24]

- A score of 30–60% may represent moderate heterogeneity
- A score of 50–90% may substantial heterogeneity
- A score of 75–100% may indicates considerable heterogeneity

Funnel plots were also used to assess for publication bias. Statistical analysis was reviewed by one of the authors who is a clinician-statistician.

Results

A PRISMA diagram is illustrated in Fig. 1. All studies were level 3 comparative retrospective studies published between 1992 and 2020. No randomized controlled trials were identified. Of the seven included studies, six were limited to paediatric patients under the age of 18 and one study was on adolescent and young adult patients with average age of 19.6 years who had high-grade high dysplastic developmental spondylolisthesis. The identified studies comprised 228 procedures of which 97 were ISF, and 131 were RFF. The average age of participants was 14.4 (Standard deviation (SD): ±2.1) years and average years of follow up was 8.2 (SD: ±5.1) years. The characteristics of each study are shown in Table 2.

Complications-pseudarthrosis

Data for pseudarthrosis and fusion rates were available from each study; however, RR calculations were not possible for Martiniani et al. due to the absence of pseudarthrosis in both groups (Fig. 2A). 9.2% (12/131) of patient undergoing RFF compared to 18.6% (18/97) of patients undergoing ISF developed pseudarthrosis. The pooled RR for developing pseudarthrosis was 0.51 (95% CI, [0.26, 0.99]) in patients undergoing RFF compared to patients undergoing ISF alone ($p=0.05$). The I^2 score was 24% and therefore can be considered of low heterogeneity.

Complications-neurological deficits

Data on all neurological complications were also available for all of the included studies (Fig. 2B). In one study there were no neurological complications, as such RR was not calculable (Burkus et al.). 11.5% (15/131) of patient undergoing RFF compared to 7.2% (7/97) of patients undergoing ISF had some type of neurological deficits. The pooled RR for developing neurological complications was 1.27 (95% CI, [0.55, 2.94]) in patients undergoing RFF compared to patients undergoing ISF alone ($p=0.58$). The I^2 score was zero.

Data on permanent neurological complications were available for five studies (Fig. 2C). In two of which there were no neurological complications, as such RR was not calculable (Burkus et al. and Poussa et al.). 5.5% (5/91) of patient undergoing RFF compared to 0% (0/62) of patients undergoing ISF had some permanent neurological deficits. Of the five patients with permanent neurological deficit, 3/5 were said to have weakness or dysaesthesia, 1/5 had injury to L5 dermatome and decreased dorsiflexion of the ipsilateral foot, and 1/5 was said to have extensor hallucis longus

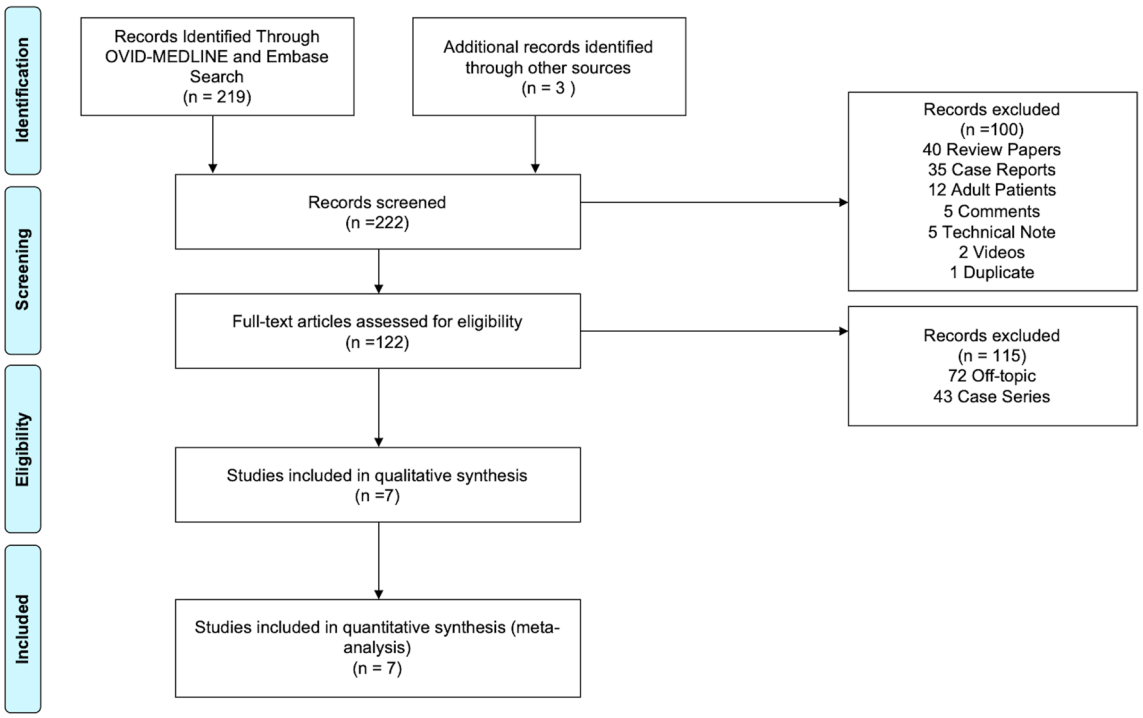

Fig. 1 PRISMA flow chart of included studies

Table 2 Characteristics of included studies

	Papers	# Patients	# In situ fusion	# Reduction	Mean age (years)	Follow up (years)	Male patients	Intervention Assessed:
1	Burkus et al. [25]	42	18	24	14	9	55%	In situ arthrodesis only. In situ arthrodesis and reduction followed by cast immobilization
2	Poussa et al. [28]	22	11	11	13.9	14.8	36%	Reduction with Magerl/Dick transpedicular screw devices and posterior fusion from L4 to S1, and 2 weeks later anteriorly L5-S1. In situ fusion L4-S1 or L5-S1 using a circumferential, anterior or posterolateral technique without instrumentation
3	Muschik et al. [27]	59	29	30	14	10.42	NS	Anterior fusion in situ Anterior spondylodesis with posterior transpedicular instrumentation and reduction
4	Molinari et al. [26]	37	12	25	13.5	3.1	38%	Posterior surgery without anterior structural support Reduction and circumferential fusion including anterior structural support
5	Poussa et al. [11]	22	11	11	14.7	14.8	27%	Fusion in situ Reduction followed by fusion
6	Martiniani et al. [29]	16	6	10	19.6	NS	44%	Fusion in situ Reduction followed by fusion
7	Rocos et al. [7]	30	10	20	14	4	NS	Instrumented fusion with partial reduction. Reduction, decompression, and instrumented fusion
		Sum: 228	Sum: 97	Sum: 131	Mean: 14.4SD: ± 2.1	Mean: 8.2SD: ± 5.1	–	–

NS Not Stated

weakness. The pooled RR for developing permanent neurological complications was 2.91 (95% CI, [0.46, 18.28]) in patients undergoing RFF compared to patients undergoing ISF alone ($p = 0.25$). The I^2 score was zero.

Complications-wound infection

Data on wound infection were available for three studies (Fig. 2D). 3.8% (3/79) of patient undergoing RFF

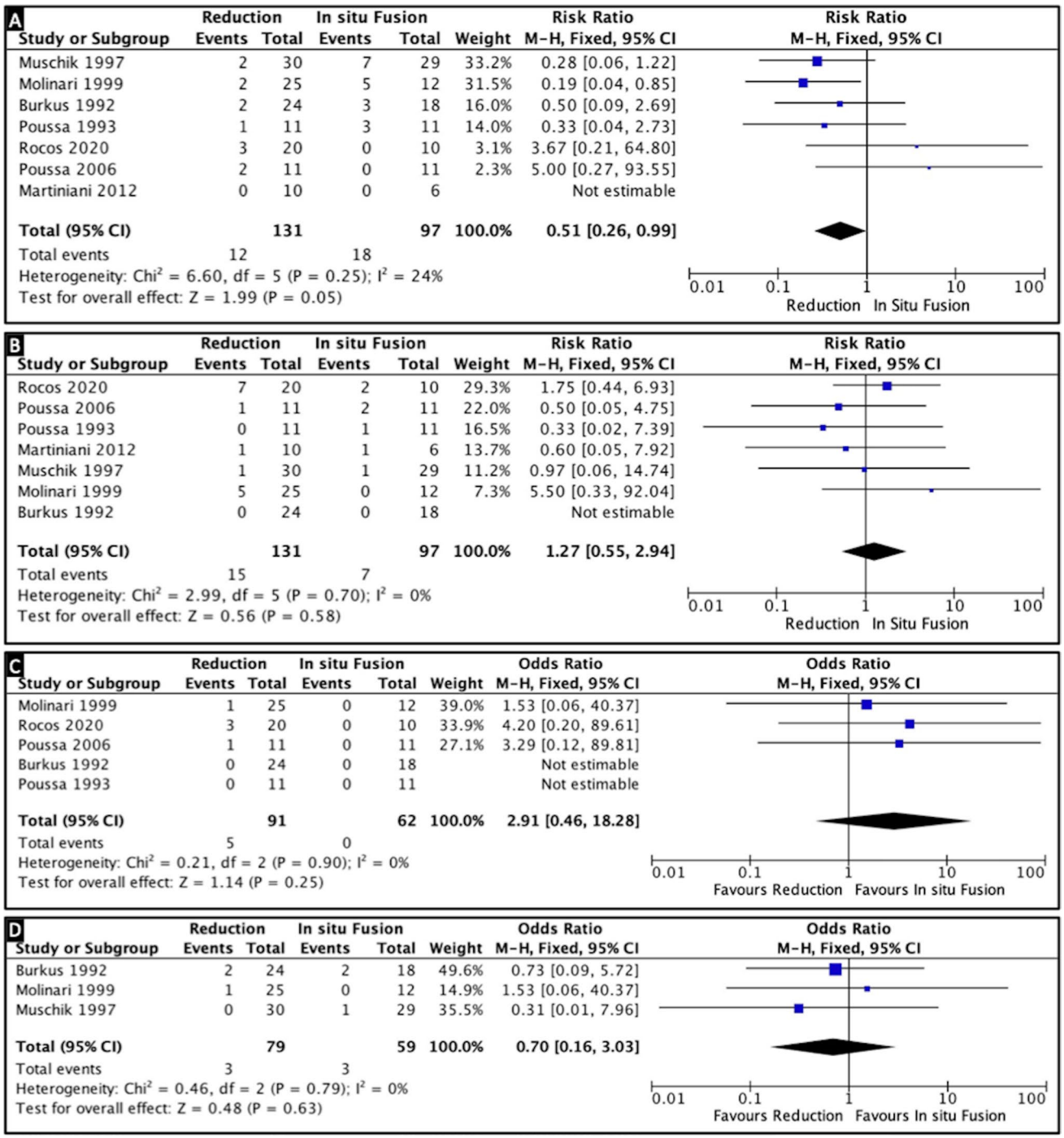

Fig. 2 Forest plot depicting the comparison of **A** Pseudarthrosis, **B** All neurological complications **C** Permanent neurological complications, **D** Wound infections, between RFF and ISF

compared to 5.1% (3/59) of patients undergoing ISF developed wound infections. The pooled RR for wound infections was 0.70 (95% CI, [0.16, 3.03]) in patients undergoing RFF compared to patients undergoing ISF alone ($p = 0.63$). The I^2 score was zero.

Reoperation

Data on reoperation were available for five studies (Fig. 3). 16.4% (18/110) of patient undergoing RFF compared to 8.8% (7/80) of patients undergoing ISF required reoperation.

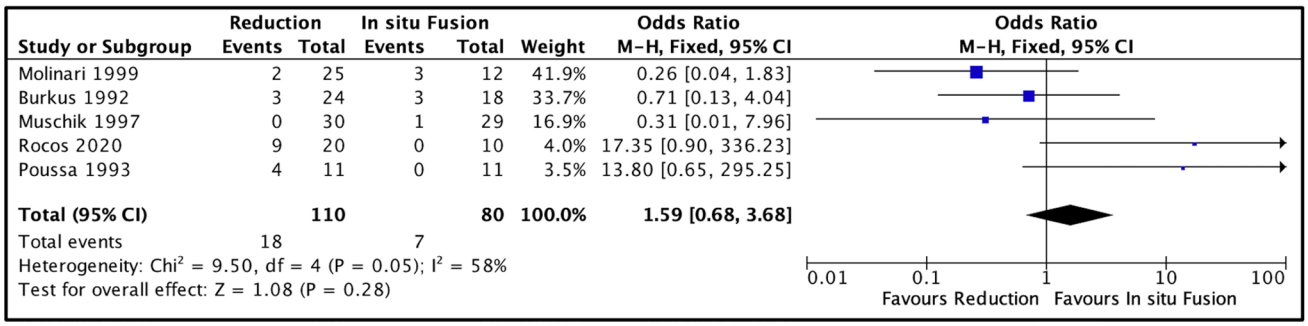

Fig. 3 Forest plot depicting the comparison of need for reoperation between RFF and ISF

The pooled RR for requiring reoperation was 1.59 (95% CI, [0.68, 3.68]) in patients undergoing RFF compared to patients undergoing ISF alone ($p=0.28$). The I^2 score was zero.

Slip angle and sagittal translation (slip percentage)

Data on slip angle were available for all of the included studies, while data on percentage of sagittal translation were available for five studies (Fig. 4). On average, the slip angle reduced 11.97° more in patients undergoing RFF compared to patients undergoing ISF alone ($p<0.0001$), however studies were substantially heterogeneous ($I^2=81\%$). Similarly, the decrease in translation was on average 34.75% larger in patients undergoing RFF compared to patients undergoing ISF alone ($p<0.00001$), although studies demonstrated substantial heterogeneity ($I^2=97\%$).

Blood loss and surgical time

Data regarding blood loss and operative time were available from two studies (Fig. 5). Average blood loss and operative time was higher in patients undergoing RFF when compared to patients undergoing ISF alone with a standardized mean difference of 1.10 (CI 95%, [0.36, 1.84], $p=0.003$) and 2.78 (CI 95%, [1.82, 3.73], $p<0.00001$), respectively. There was low heterogeneity ($I^2=8\%$ and $I^2=0\%$, respectively) when comparing both blood loss and operative time standardized mean differences.

Summary of all results are shown in Table 3.

Subjective patient satisfaction

Subjective patient satisfaction data were available for 4 studies. OR calculations could not be done for Molinari et al. as

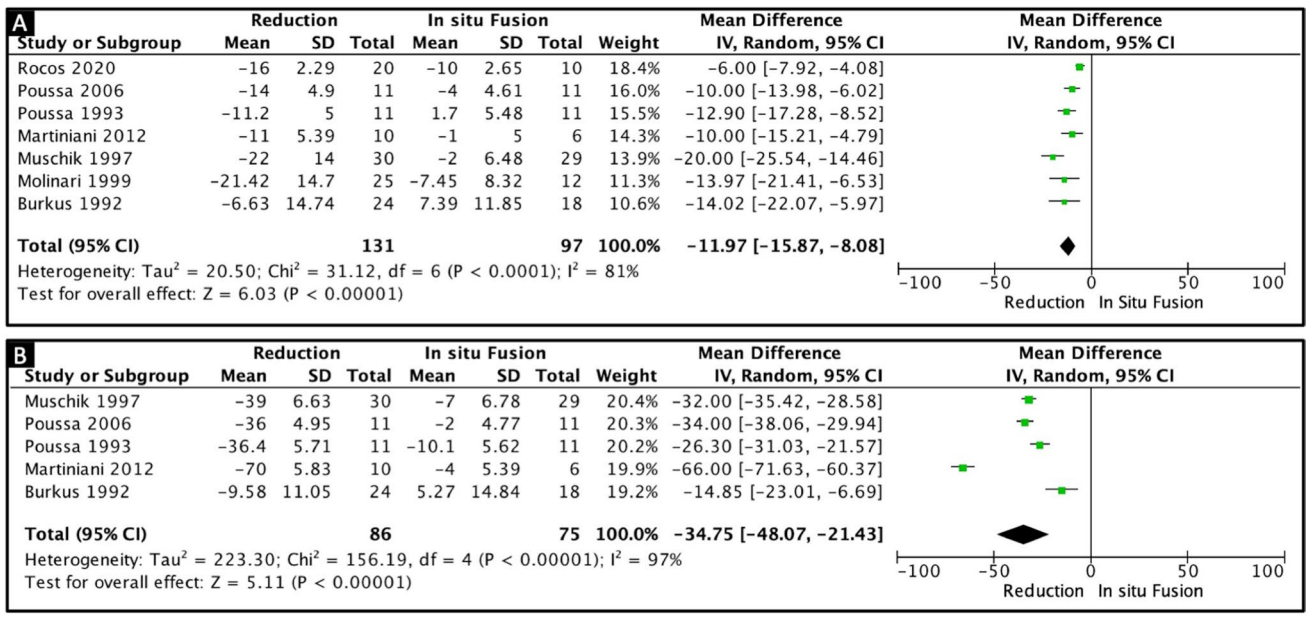

Fig. 4 Forest plot depicting the comparison of **A** Slip angle, **B** Per cent of sagittal translation, between RFF and ISF

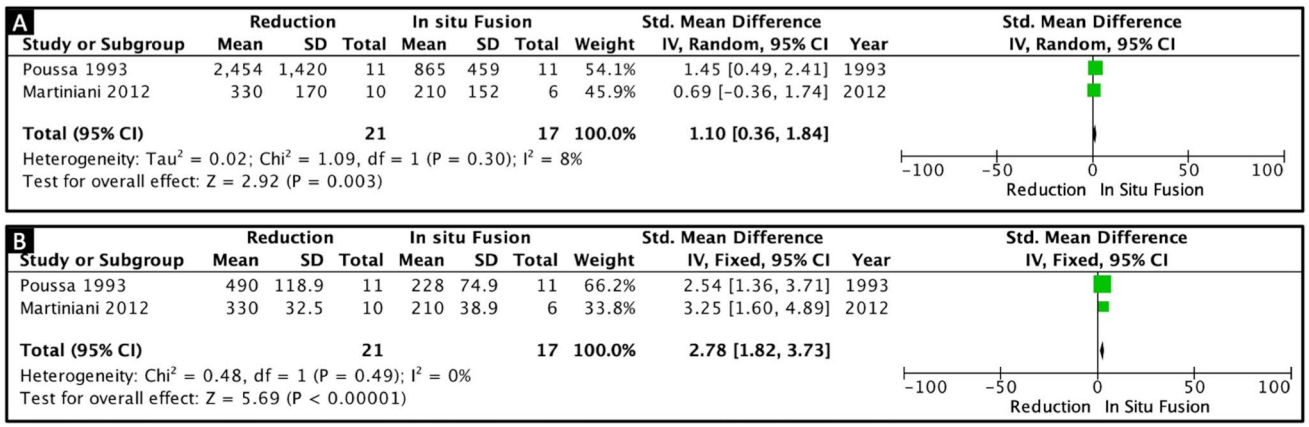

Fig. 5 Forest plot depicting the comparison of **A** Intraoperative blood loss, **B** Surgical time, between RFF and ISF

Table 3 Summary of Results

	Reduction	Fusion	Reduction vs. Fusion	Significance
Patients Not Satisfied	13.3% (10/75)	11.9% (7/59)	OR 1.47 [0.52, 4.16])	$p=0.47$
Pain on Follow Up	18.8% (16/85)	23.5% (16/68)	OR 0.78 [0.41, 1.49]	$p=0.46$
Pseudarthrosis	9.2% (12/131)	18.6% (18/97)	RR: 0.51 [0.26, 0.99]	$\mathbf{p=0.05}$
Overall Neurological Complications	11.5% (15/131)	7.2% (7/97)	RR: 1.27 [0.55, 2.94]	$p=0.58$
Permanent Neurological Complications	5.5% (5/91)	0% (0/62)	2.91 [0.46, 18.28]	$p=0.25$
Wound Infection	3.8% (3/79)	5.1% (3/59)	0.70 [0.16, 3.03]	$p=0.63$
Reoperation	16.4% (18/110)	8.75% (7/80)	1.59 [0.68, 3.68]	$p=0.28$
Average Decrease in Slip Angle	−15.7°	−2.3°	MD: −11.97° [−15.87°, −8.08°]	$\mathbf{p<0.0001}$
Average Decrease in Sagittal Translation	−33.7%	−3.5%	MD: −34.75% [−48.07%, −21.43%]	$\mathbf{p<0.00001}$
Average Blood Loss	1442.6 mL	633.9 mL	SMD: 1.10 [0.36, 1.84]	$\mathbf{p=0.003}$
Average Surgical Time	413.8 min	221.6 min	SMD: 2.78 [1.82, 3.73]	$\mathbf{p<0.00001}$

Statistically significant results highlighted in bold

OR Odds ratio, *RR* Risk ratio, *MD* Mean difference, *SMD* Standard mean difference

all patients in both groups were satisfied (Fig. 6A). 86.7% (65/75) of patient undergoing RFF compared to 88.1% (52/59) of patients undergoing ISF expressed satisfaction. The OR for patients not being satisfied was 1.47 (95% CI, [0.52, 4.16]) for patients undergoing RFF compared to patients undergoing ISF alone ($p=0.47$). The I^2 score was zero.

Pain on follow up

Data on lower back pain or pain radiating to legs were available for 4 studies (Fig. 6B). 18.8% (16/85) of patient undergoing RFF compared to 23.5% (16/68) of patients undergoing ISF had lower back pain or pain radiating to their legs at follow up. The OR for experiencing lower back or leg pain was 0.78 (95% CI, [0.41, 1.49]) for patients undergoing RFF compared to patients undergoing ISF alone ($p=0.46$). The I^2 score was zero.

Rik of bias

All studies displayed moderate to severe risk of bias for all outcomes and were of low to moderate quality. Visually, funnel plots comparing reduction and ISF showed no substantial publication bias (Fig. 7). All of the included level 3 studies had a moderate to serious risk of outcome bias and as such each earned a GRADE quality score of moderate to low.

Discussion

In this report, we have performed a meta-analysis using data extracted from seven level 3 retrospective studies to compare outcomes of RFF versus ISF for paediatric HGS. Although

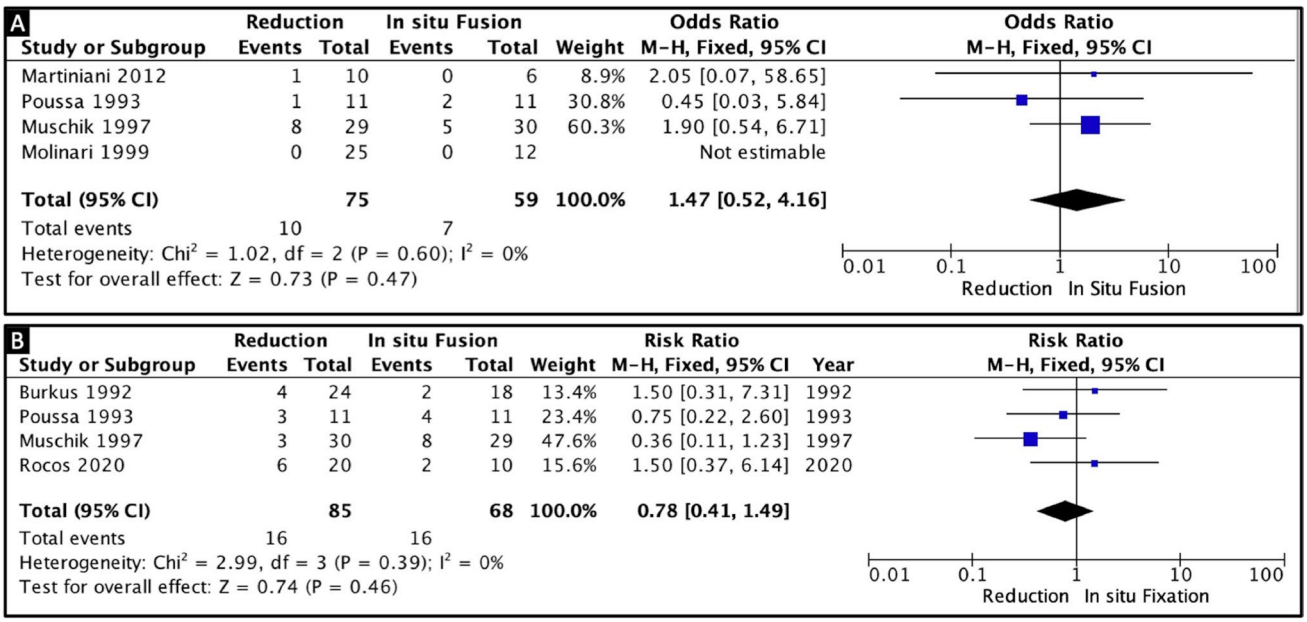

Fig. 6 Forest plot depicting the comparison of **A** Subjective patient satisfaction, **B** Lower back pain or leg pain, between RFF and ISF

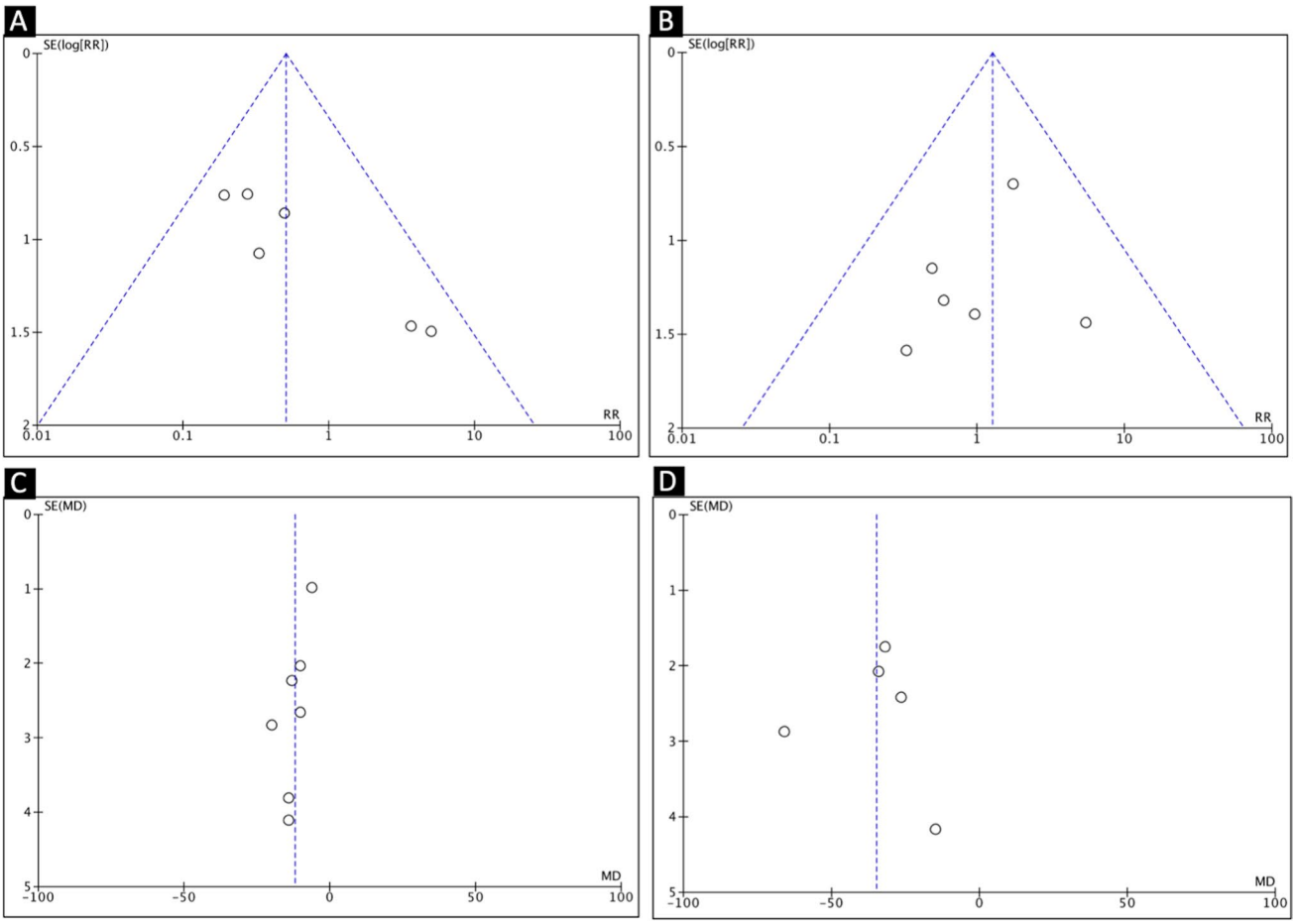

Fig. 7 Funnel plots comparing reduction and in situ fusion. **A** Pseudarthrosis, **B** Neurological complications, **C** Slip angle, **D** Sagittal translation

RFF procedures had significantly longer surgical times and more intraoperative blood loss, both strategies are effective and lead to desirable outcomes for HGS in paediatric and young adult patients. Patients undergoing RFF procedures were more likely to require re-operation, whereas wound infections were more frequent in ISF procedures, however these differences were not significant.

Surgical options for the management of HGS include fusing the affected motion segment in place or reducing the translation and angular deformity followed by fusion [7]. Despite several attempts, which of these strategies gives superior outcomes remains undefined in the paediatric and young adult age groups [7, 11, 18, 25–29]. Previous meta-analyses have either focussed entirely on adult patients or have performed pooled data analysis without separating studies of paediatric patients.

Paediatric, adolescent, and young adult patients with spondylolisthesis are different from adult patients. The aetiology of HGS in paediatric and young adult patients is typically due to traumatic, congenital, and/or developmental defects leading isthmic or dysplastic spondylolisthesis, whereas HGS in adult and older patients is more frequently degenerative [30].

It is important to note that both RFF and ISF procedures led to comparable subjective satisfaction results (86.7% for reduction and 88.1% for ISF, without any significant difference). Additionally, there was not a significant difference between lower back pain and pain radiating to legs between RFF and ISF. However, these findings are limited by the small sample size.

Pseudarthrosis

We found that patients undergoing RFF compared to patients undergoing ISF alone were 49% less likely to develop pseudarthrosis (95% CI, [0.26, 0.99], $p = 0.05$). This is similar to the findings of Longo et al. who used pooled data from paediatric and adult patients with HGS undergoing RFF to show a 59% reduction in the relative risk of developing pseudarthrosis compared to the arthrodesis in situ [18]. In a meta-analysis by Jiang et al., using data from mixed populations of paediatric and adult patients with high-grade and low-grade spondylolisthesis, it was shown that reduction significantly improved fusion rates [19]. Based on these and our own conclusions, there appears to be consensus on the argument that RFF improves overall fusion rates compared to ISF alone in paediatric and young adult patients.

Neurological complications

Post-operative neurological complications could result from either direct injury to nerves or traction of nerve roots during reduction manoeuvers [27, 31, 32]. Our data show that patients undergoing RFF were more likely to develop neurological complications than those undergoing ISF, however this difference was not statistically significant. Of note, 5.5% of patient undergoing RFF compared to none of patients undergoing ISF had permanent neurological deficits. Similarly, Longo et al. found that neurological complications were more frequently seen with the reduction group, however again this finding was not statistically significant [18]. Petraco et al. found that in patients with HGS undergoing reduction, the majority of stretch injury to the L5 nerve occurs during the second half of reduction, and suggested that partial reduction may be a significantly safer approach [33]. In contrast, another study found that neurological complications were more frequent with in situ arthrodesis, although not statistically significant [20]. Schär et al. found that transient L5 radiculopathy after reduction of HGS is frequent, however, the radiculopathy resolves by three months and patient-reported outcomes showed significant improvements for patients with and without L5 radiculopathy [34]. Although not statistically significant, there appears to be clinically more lasting neurological injury with RFF compared to ISF.

Spinopelvic parameters

It has been previously suggested that slip angle is the most important determinant of pseudarthrosis and pain [35]. Larger pre-operative slip angles are also correlated with higher rates of implant failure and post-operative radiculopathy [36]. In line with previous studies, RFF compared to ISF alone, led to about 12° more of reduction in slip angle and 35% more reduction in sagittal translation ($p < 0.00001$). Longo et al. also found a significant decrease in slip angle and a larger decline in sagittal translation in the reduction group [18]. Comparably, Jiang et al. and Lak et al. also showed a more significant decrease in the slip angle for the reduction group [19, 20]. Reduction restores the vertebrae into a more anatomic alignment and by reducing the slip grade it could increase the area available for interbody fusion [14, 16]. It can therefore be argued that reducing the translated vertebra led to improved spinal biomechanics, which ultimately led to the improved fusion rates observed in this group [7, 15, 37]. However, 3D finite element studies have shown that reducing the translation onto a balanced pelvis has minimal effects on the mechanical conditions of the adjacent segments, while reduction of unbalanced cases creates stress concentration on adjacent levels, so compromising the fusion environment [16]. It should be noted that the relationship between improved biomechanics and fusion rates are mostly speculative, and further investigations are required.

Strengths and limitations

Strengths of this analysis include a comprehensive search strategy, absence of publication bias, and low heterogeneity for many outcomes presented. There are some limitations to this analysis. A single study investigating adolescent and young adult patients with high-grade high dysplastic developmental spondylolisthesis was included because this patient population physiologically resembles paediatric age groups.

Moreover, the analysis was unable to differentiate between results of unbalanced and balanced HGS due lack of data from the included studies. Furthermore, studies were not stratified based on instrumentation, such as interbody graft and pedicle screws, due to significant heterogeneity present and lack of outcome stratification based on instrumentation. Another limitation is that we are unable to comment on the types of neurologic deficits due to lack of consistent reporting. Pain and disability ratings were heterogeneously reported. To further compare these two surgical procedures these patient-reported outcomes should be considered. Therefore, we recommend that future studies include longer term patient satisfaction scores and standard validated pain and disability rating scales in addition to assessment of the complications and changes to spinopelvic parameters.

All of the included level 3 studies had a moderate to serious risk of outcome bias and as such each earned a GRADE quality score of moderate to low. Therefore, the results of this meta-analysis should be interpreted with caution and highlights the need for better quality studies.

Conclusion

Surgical management of HGS in symptomatic paediatric patients is challenging. Both RFF and ISF are effective techniques for managing HGS. While RFF is more effective in restoring slip angle, it was associated with an increased risk of transient and permanent neurological complications in young patients, however this difference was not significant. Correlation with patient-reported outcomes still needs to be further explored.

Finding

None.

Declarations

Conflicts of Interest Conflict of interest statement None of the authors has any potential conflict of interest.

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